UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte ELIZABETH M. DENHOLM, YONG-QING LIN and PAUL J. SILVER

Appeal No. 2004-2186
Application No. 09/715,965

HEARD: January 11, 2005

Before WILLIAM F. SMITH, SCHEINER and GRIMES, Administrative Patent Judges.

SCHEINER, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the final rejection of claims 1-11 and 19-27, the only claims remaining in the application.

Claims 1, 4, 6 and 8 are representative:

1. A method to decrease angiogenesis comprising administering to a site in an individual in need of treatment thereof for an established disorder requiring angiogenesis an effective amount of a purified chondroitinase to decrease angiogenesis at the site, wherein the decrease in angiogenesis is measured as a decrease in endothelial cell proliferation or a decrease in the formation of capillary-like structures.

4. The method of claim 8 wherein the enzyme is a chondroitinase AC.

6. The method of claim 1 wherein the enzyme is administered to an individual having cancer as evidenced by palpable tumors.

8. The method of claim 1 wherein the individual has a disorder in which angiogenesis is involved, the disorder being selected from the group consisting of rheumatoid arthritis; psoriasis; ocular angiogenic disease, rubeosis, Osler-Webber Syndrome; myocardial angiogenesis; plaque neovascularization; telangiectasia; hemophiliac joints; angiofibroma; Crohn's disease, atherosclerosis, scleroderma, hypertrophic scarring, adhesions, cirrhosis of the liver, pulmonary fibrosis following acute respiratory distress syndrome or other pulmonary fibrosis of the newborn, endometriosis, polyposis, obesity, uterine fibroids, prostatic hypertrophy, and amyloidosis.

The examiner relies on the following references:

Brown	4,696,816	Sep. 29, 1987
Sasisekharan et al. (Sasisekharan)	5,567,417	Oct. 22, 1996

Takeuchi, "Effect of Chondroitinases on the Growth of Solid Ehrlich Ascites Tumor," Br. J. Cancer, Vol. 26, pp. 115-119 (1972)

The claims stand rejected as follows:

I. Claims 1-11 and 19-27 under 35 U.S.C. § 112, first paragraph, as lacking written descriptive support.

II. Claims 1-11 and 19-27 under 35 U.S.C. § 112, first paragraph, as lacking enablement.

III. Claims 1-11 and 19-27 under 35 U.S.C. § 112, second paragraph, as indefinite.

IV. Claims 1, 2, 4, 5, 9, 10 and 27 under 35 U.S.C. § 102(b) as anticipated by Takeuchi.

V. Claims 1, 2, 4-6 and 8 under 35 U.S.C. § 102(b) as anticipated by Brown.

VI. Claims 1-11 and 19-27 under 35 U.S.C. § 103 as unpatentable over Sasisekharan together with Takeuchi or Brown.

VII. Claims 1-11 and 19-27 under 35 U.S.C. § 103 as unpatentable over Takeuchi or Brown.

We reverse these rejections.

PROCEDURAL MATTER

Apparently, appellants and the examiner agreed on an election of species early in the prosecution of this application, both parties confirming that examination would be initially limited to treatment of cancer with chondroitinase-AC (see the non-final office action mailed August 13, 2001, and appellants' response mailed November 13, 2001). Nevertheless, the claims appear to have been examined across their full scope (see the enablement rejection of claims 1-11 and 19-27 in particular). For this reason, in deciding the issues on appeal, we have considered the claims and the rejections without regard to the earlier election of species.

BACKGROUND

"Angiogenesis, the proliferation and migration of endothelial cells that result[s] in the formation of new blood vessels, is an essential event in a wide variety of normal and pathological processes. For example, angiogenesis plays a critical role in embryogenesis, wound healing, psoriasis, diabetic retinopathy, and tumor formation" (Specification, page 11).

According to the specification (pages 2-3), chondroitinases "can be used in the treatment of metastatic cancers. The enzymatic removal of chondroitin sulfates . . . from tumor cell surfaces effectively A) decreases their ability to proliferate when stimulated by oncogenic growth factors, B) decreases the ability of tumor cells to invade blood vessels and thus prevents the formation of metastatic, or secondary tumors, and C) decreases angiogenesis by inhibiting both endothelial cell proliferation and capillary formation." "Decreasing the formation of new blood vessels into the tumor in turn

decreases the potential for tumor growth, and further decreases the ability of tumor cells to invade the bloodstream. These anti-metastatic effects of chondroitinases are opposite to the pro-metastatic effects of tumor secreted heparanases" (id., page 3).

The specification also teaches that chondroitinases can be used to treat a variety of "other disorders involving angiogenesis including rheumatoid arthritis; psoriasis; ocular angiogenic diseases; [etc.]; and diseases that have angiogenesis as a pathologic consequence" (id., page 10).

DISCUSSION

I. Written Description

Compliance with the written description provision of 35 U.S.C. § 112, first paragraph requires sufficient information in the original disclosure to show that the inventor possessed the invention at the time of the original filing. See Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1561, 19 USPQ2d 1111, 1115 (CAFC 1991) ("Adequate description of the invention guards against the inventor's overreaching by insisting that he recount his invention in such detail that his future claims can be determined to be encompassed within his original creation"). Stated differently, applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. "The written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [applicant] invented what is claimed.'" Union Oil Co. of Cal. v. Atlantic Richfield Co., 208 F.3d 989, 997, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000) (citation omitted).

According to the examiner, "[t]here is no support for the term[ ] 'an established disorder requiring angiogenesis'" (Answer, page 4). We disagree. In our view, one of ordinary skill in the art would readily recognize that Example 9 (Specification, pages 19-20), wherein mice with palpable tumors were treated with chondroitinase AC, describes treatment of an "established" angiogenesis-dependent disorder. Moreover, several of appellants' original claims explicitly require administration of a chondroitinase to an individual with an established disease (e.g., original claim 6, "wherein the individual has cancer" and original claim 8, "wherein the individual has a disorder in which angiogenesis is involved, the disorder being selected from the group consisting of rheumatoid arthritis, psoriasis, [etc.]").

The examiner has failed to establish that one of ordinary skill in the art would not have recognized that appellants, as of the filing date, invented what is claimed. The rejection of the claims for lack of written description under the first paragraph of 35 U.S.C. § 112 is reversed.

II. Enablement

"The first paragraph of 35 U.S.C. § 112 requires, inter alia, that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention. Although the statute does not say so, enablement requires that the specification teach those in the art to make and use the invention without 'undue experimentation.' In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). That some experimentation may be required is not fatal; the issue is whether the amount of experimentation is 'undue.'" In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d

1438, 1444 (Fed. Cir. 1991) (emphasis in original).[1] Nevertheless, "[w]hen rejecting a claim under the enablement requirement of section 112," it is well settled that "the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement." In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

Thus, the issue here is not whether appellants have established that the disclosure is broadly enabling for the scope of the claims; the issue is whether the PTO has met its "initial burden of setting forth a reasonable explanation as to why" it is not.

The examiner rejected claims 1-11 and 19-27 under 35 U.S.C. § 112, first paragraph, because "[t]he specification as filed, is enabled for reducing tumor cell growth using a chondroitinase, but is not enabled for treating an established disorder requiring angiogenesis" (Answer, page 5). The examiner argues that "[t]he art of biotechnology is a highly unpredictable art and it would be an undue burden for one of

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[1]

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman [230 USPQ 546, 547 (BdPatAppInt 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims (footnote omitted).

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

ordinary skill in the art to test if an established disorder requiring angiogenesis can be treated with the enzyme" (id.) because "[d]isorders such as arthritis and atherosclerosis, obesity in and of themselves are unrelated and one would not make the connection of them to the enzyme with only knowing that tumors could be reduced with the enzyme since different disorders are effected differently with different treatments" (id., page 5).

In our view, the reasons given by the examiner in support of the enablement rejection do not provide an adequate basis to question the adequacy of appellants' disclosure. First, it is not clear why claims 6, 7, 19 and 21 were included in this rejection since each is directed to treatment of "an individual having cancer as evidenced by palpable tumors." This might have been an oversight, or it might reflect the examiner's concern that the results of in vitro inhibition of tumor cell lines might not be predictive of in vivo results. If so, it is not clear why the examiner did not comment on any of the examples in the specification, e.g., Example 6, directed to formation of capillary-like structures (CLS), or Example 9, directed to chondroitinase treatment of mice exhibiting palpable tumors.

Second, with respect to treatment of disorders other than cancer and/or tumors, the specification teaches that many otherwise unrelated disorders (e.g., rheumatoid arthritis; psoriasis; ocular angiogenic disease, adhesions, endometriosis, uterine fibroids, etc.) are similar to each other in that they require angiogenesis for their establishment or maintenance. The examiner, in focusing on the differences between these disorders, appears to have overlooked or disregarded this commonality, even though the specification teaches that this commonality can be exploited to decrease disease progression in a number of otherwise unrelated diseases.

In short, on this record, the examiner has not provided a factual basis to support his conclusion that the claims are not enabled by the specification. The rejection of claims 1-11 and 19-27 for lack of enablement under 35 U.S.C. § 112, first paragraph, is reversed.

III. Indefiniteness

The examiner rejected claims 1-11 and 19-27 as indefinite under 35 U.S.C. § 112, second paragraph, because "[i]t is not clear what applicant[s] [are] referring to when they state, 'these enzymes expressed from recombinant nucleotide sequences in bacteria'" (Answer, page 6).

We find this rejection to be without merit. First, the language criticized by the examiner appears only in claim 2. Second, appellants argue that "one skilled in the art would know that the enzymes referred to in claim 2 are normally expressed by the named bacteria, [that] all of these enzymes have been cloned, [and] one could also express the same [enzymes] in a different organism" (Reply Brief, page 7).

"[T]he definiteness of the language employed [in a claim] must be analyzed - - not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art." In re Moore, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (CCPA 1971). With that in mind, we find appellants' position to be a reasonable one. The rejection of claims 1-11 and 19-27 under 35 U.S.C. § 112, second paragraph, is reversed.

IV and V. Anticipation

Claims 1, 2, 4, 5, 9, 10 and 27 were rejected under 35 U.S.C. § 102(b) as anticipated by Takeuchi. Takeuchi describes subcutaneous injection of mice with chondroitinase-AC, "immediately followed by injection of 0.05 ml of [ ] Ehrlich tumour ascitic fluid, containing $1x10^7$ cells. Controls were injected with isotonic saline before the tumour inoculation. Animals were killed on the 8^{th} day after tumour inoculation, and the solid tumour which developed subcutaneously was excised and weighed" (pages 115-116).

We agree with appellants that Takeuchi does not describe administering chondroitinase to a subject with an established disorder requiring anigiogenesis, inasmuch as the enzyme was administered before the tumor cells were injected.

Claims 1, 2, 4-6 and 8 were rejected under 35 U.S.C. § 102(b) as anticipated by Brown. Brown describes treating intervertebral disc displacement by injecting chondroitinase into the intervertebral disc space, and briefly mentions that "[t]he enzyme's pharmaceutical use is not limited to nucleus pulposus, but should find application in the treatment of ganglia, arthroscopy of joints, certain eye conditions, tumors, and other unwanted cartilage tissue" (Column 4, lines 42-45).

According to the examiner, "[s]ince Brown teaches treating tumors this would include individuals with cancer and thus decreasing angiogenesis. When the enzyme is applied to the tumor it will inherently perform the claimed process" (Answer, page 7).

Brown's brief comment about treatment of tumors notwithstanding, we find no suggestion in Brown to inject chondroitinase into anything other than cartilaginous tissue, and, as appellants point out, "cartilaginous tissue is avascular" (Brief, page 15).

In our view, the examiner has not identified evidence sufficient to shift the burden to appellants to establish that Brown's method does not inherently inhibit angiogenesis.

The rejection of claims 1, 2, 4, 5, 9, 10 and 27 as anticipated by Takeuchi is reversed, as is the rejection of claims 1, 2, 4-6 and 8 as anticipated by Brown.

VI and VII. Obviousness

Claims 1-11 and 19-27 were rejected under 35 U.S.C. § 103 as unpatentable over Sasisekharan taken with Takeuchi or Brown. Sasisekharan describes inhibiting angiogenesis, in various disorders that require angiogenesis, by administering heparinases. The examiner's position is that "it would have been obvious to one of ordinary skill in the art to use a chondroitinase instead of a heparinase for decreasing angiogenesis" since both Brown and Takeuchi teach that "it is known to treat tumors and cancerous tumors with chondroitinase" and "both of the references clearly show beneficial results" (Answer, page 8).

Nevertheless, we see no nexus between Sasisekharan and Takeuchi or Brown, as neither of these latter references mentions angiogenesis at all. Nor is there anything on the record to indicate that heparinases and chondroitiases would have been regarded as interchangeable by one skilled in the art at the time of the invention.

Finally, the examiner rejected claims 1-11 and 19-27 under 35 U.S.C. § 103 as unpatentable over Takeuchi or Brown. The examiner concedes that neither reference teaches "specific amounts of the enzyme to be used" (Answer, page 8), but asserts that administering chondroitinase "at different concentrations is simply the choice of the artisan in an effort to optimize the desired results" (id.).

We disagree. As discussed above, the claims require administration of chondroitinase to an individual with an established disorder which requires angiogenesis – something neither Takeuchi nor Brown describes. Moreover, the claims require administration of chondroitinase at a site in an amount effective to inhibit angiogenesis at the site. Since neither Takeuchi nor Brown mentions angiogenesis, we see nothing in either reference to suggest the required amounts.

The rejection of claims 1-11 and 19-27 as unpatentable over Sasisekharan taken with Takeuchi or Brown is reversed, as is the rejection of claims 1-11 and 19-27 as unpatentable over Takeuchi or Brown.

CONCLUSION

For the reasons stated above, we reverse rejections I- VII.

REVERSED

William F. Smith
Administrative Patent Judge)

Toni R. Scheiner) BOARD OF PATENT
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